# Assessing the effectiveness of the NCI's Alliance initiative in generating high impact scientific outputs and enabling clinical translation of nanotechnologies developed in academia

Natalie Abrams, Christopher Belter, James G. Corrigan, Elizabeth R. Hsu, Ya-Ling Lu, Alan L. Porter, Piotr Grodzinski

#### Summary

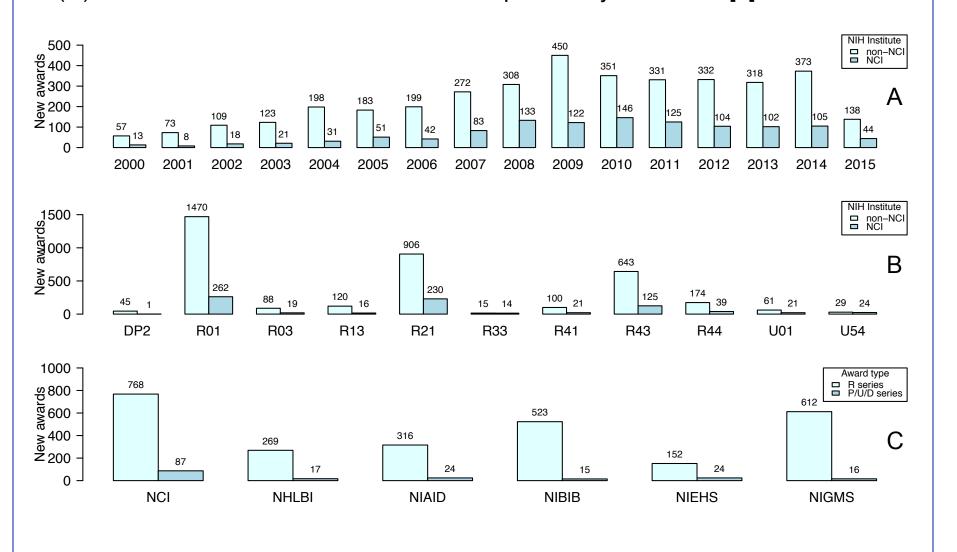
Here we assess the relative effectiveness of the team science structure supported by the NCI's Alliance for Nanotechnology in Cancer (<a href="http://nano.cancer.gov/">http://nano.cancer.gov/</a>) in (i) generating high-impact scientific publications, (ii) facilitating multi-disciplinary collaborations, and (iii) enabling clinical translation of nanotechnologies developed in academia. Research outputs from the Alliance network were compared to those supported by R01 grants matched by start dates and research focus. Although all groups demonstrated similar productivity and citation impact per \$1M of direct funding, the Alliance network was shown to be especially effective in driving interdisciplinarity among investigators and in facilitating clinical translation of nanotechnologies.

#### Background

#### NIH investment in Nanotechnology

Over the past decade at the National Institutes of Health (NIH) has invested \$450M per year into nanotechnology-focused research and training programs including over \$150M per year provided by the National Cancer Institute (NCI) alone (Fig.1). Other institutes with significant level of support include NHLBI, NIAD, NIBIB, NIEMS and NIGMS. The number of new awards has grown accordingly, with R01 being most common awards type as shown in Fig. 1.

**Figure 1.** Distribution of new awards and competing renewals in the area of nanotechnology across time (A), funding mechanism (B), and NIH institute (C). Award-related data were collected as previously described [1].



#### The NCI Alliance for Nanotechnology in Cancer

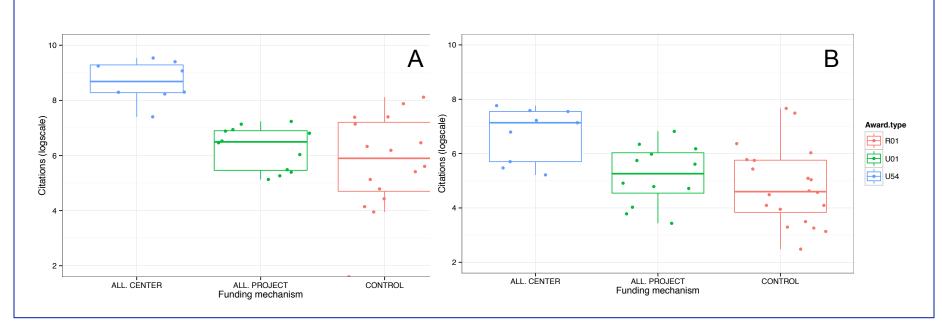
In 2004, NCI launched the Alliance for Nanotechnology in Cancer initiative, which has supported a virtual network of cancer nanotechnology centers and individual projects. The network has provided opportunities for collaborations with other Alliance members, industry partners, and the intramural Nanotechnology Characterization Laboratory (<a href="http://ncl.cancer.gov">http://ncl.cancer.gov</a>). To facilitate information sharing, the Alliance also established a data-sharing portal, caNanoLab (<a href="https://cananolab.nci.nih.gov">https://cananolab.nci.nih.gov</a>).

#### Results

#### High-impact scientific output from the Alliance network

In order to compare research outputs of the Alliance network and unsolicited grants, we developed three cohorts. The two test cohorts were comprised of U01/R01 and U54 awards funded through the Alliance initiative in 2005 and 2010. The control group was comprised of nanotechnology focused R01s grants awarded as new grants in 2005 or 2010. Although Alliance investigators generated more publications and citations than Controls, all groups demonstrated similar productivity and citation impact per \$1M of direct funding. Figure 2 shows that despite significant dispersion in citations numbers and the overall increase in citations accumulated for Phase I awards, similar citation trends observed in phases I (2005-2009) and II (2010-2014).

**Figure 2.** Citations of publications supported by the Alliance and Control awards during phase I (2005-2009; panel A) and II (2010-2014; panel B).

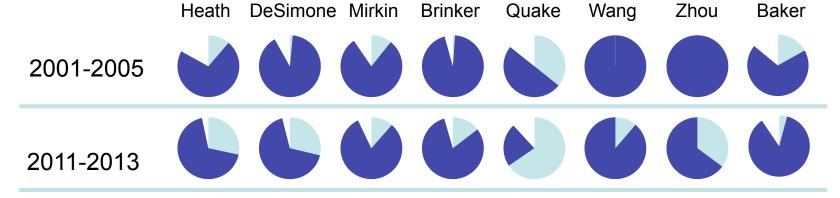


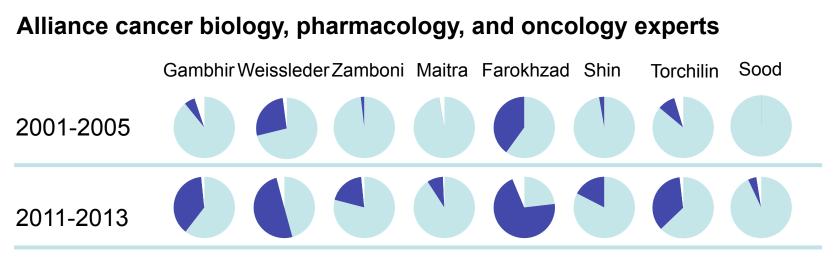
#### **Cross-disciplinary mobility among Alliance investigators**

To better understand the impact of the award on cross-disciplinary mobility of Alliance PIs, we categorized their publications before and after receiving the award (2010) as cancer or nanotechnology focused. The observed patterns showed a marked shift towards a more interdisciplinary profile (Fig. 3), highlighting the relevance of the Alliance network in driving interdisciplinarity.

**Figure 3.** Topical distribution of publications authored by 16 most productive Alliance investigators [2]. Color code: pale blue – biomedical, dark blue – nanotechnology, white – other.

### Alliance nanotechnology experts



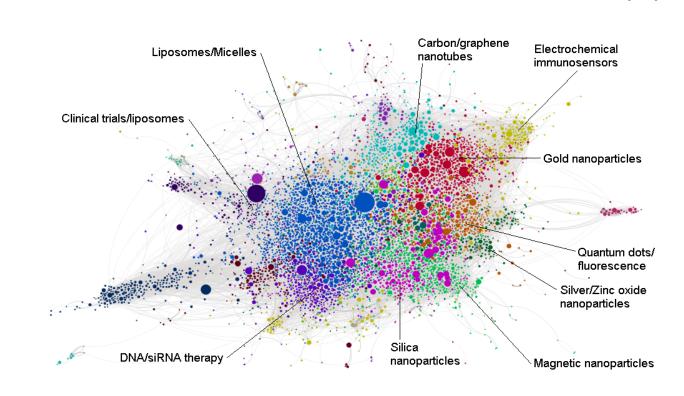


## Distribution of Alliance publications across research topic, medical application, disease, and translational stage

To better understand the impact of the Alliance network on clinical translation of nanotechnologies, we first wanted to categorize the awards based on research topic, medical application, and human disease, because translational research milestones can vary depending on the nature of research.

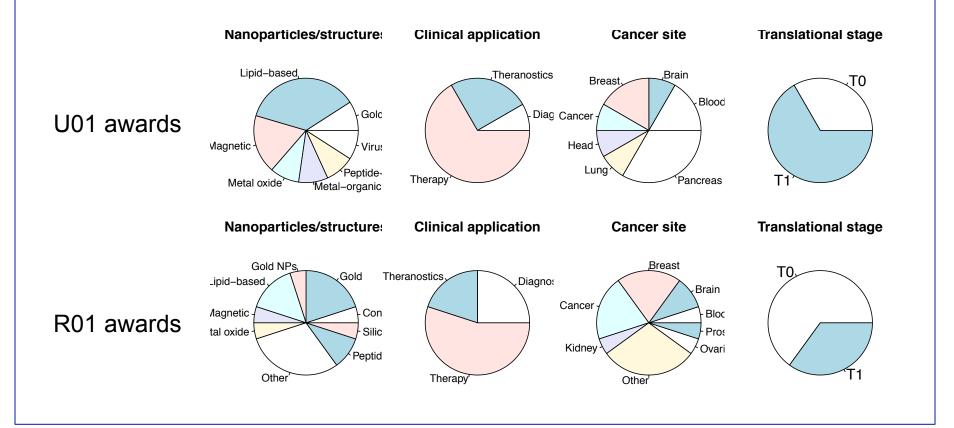
To that end, we identified most active topics in cancer nanotechnology by analyzing co-citation relationships among ~6,000 journal articles published in 2013. Figure 4 shows the top ten publication clusters identified in this dataset. Thematic analysis of publication abstracts in these clusters demonstrated that each cluster had one dominant nanotechnology theme. Notably, subsequent citation analysis identified three highly active areas (gold, carbon/graphene, and silica nanoparticles), which received many citations in less than a year.

Figure 4. A bibliometric map of cancer nanotechnology (2013). Each dot (node) represents an original research paper; the dot's color indicates its algorithmically-derived cluster; and the dot's size indicates its citation count received in 2014. Lines indicate shared references between two papers.



This information allowed us to categorize Alliance awards based on the type of nanotechnology described in application abstracts. Figure 5 shows that, during phase II, Alliance U01 applications were mostly focused on lipid-based nanoparticles, while controls which were dominated by gold nanoparticles. Also, in comparison to R01 grants, more Alliance awards were categorized as therapy-focused vs. diagnostics-or theranostics-focused. Finally, in contrast to R01 grants, the majority of Alliance awards progressed further along the translation pipeline, consistent with the program goal to facilitate clinical translation of nanotechnologies developed in academia.

**Figure 5.** Distribution of Alliance (U01) and control (R01) awards across nanomaterial, clinical application, disease, and translational stage categories.



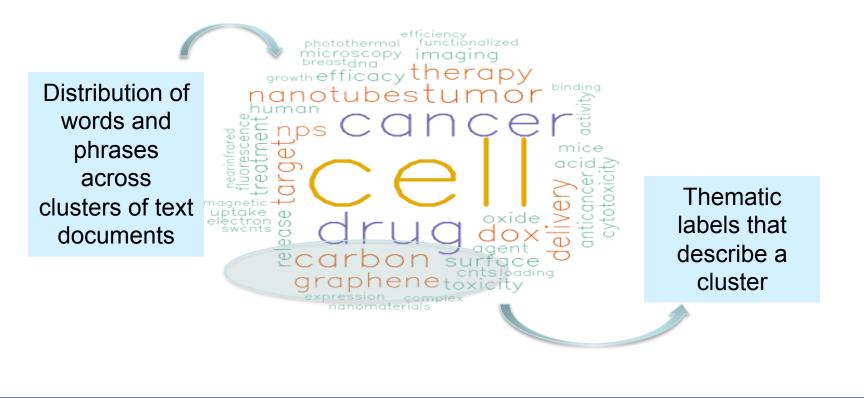
#### Methods used for topic modeling

**Lexical query.** To build a topic map, ~6,000 original research articles published in 2013 were collected from the WoS Core Collection [3] using a lexical query incorporating "nano\*" and cancer-related terms, but excluding irrelevant terms such as nanometer. Only original-research journal articles were included in the analysis.

Research community topic modeling and bibliometric mapping. The publications were clustered into 10 groups using Bibliographic Coupling, which is a similarity measure based on the number of shared references within publications. If two papers share one or more bibliographic references, they are assumed to be topically related and get clustered together. Once distance measures are calculated for each publication pair, the relationships among publications are visualized as a network-based bibliometric map, where nodes represent the individual publications, and edges represent the distance between two nodes. The network analysis was performed using the Science of Science tool (Sci2) and visualization using Gephi.

Thematic labeling of publication clusters. Top ten publication clusters were labeled by representative nouns and phrases found in publication abstracts. First, most frequent terms were identified by comparing the distributions of words and phrases using the tm package in R. Then, for each cluster, top candidate labels were manually reviewed to find terms not present in other clusters (Fig. 6).

**Figure 6.** Process example: Selecting a thematic label for the Carbon/ Graphene nanoparticle cluster. This is a graphic representation of the semi-supervised selection process in which unique, representative labels are selected from a list of most frequent terms and phrases found in clusters of text documents (e.g. publication or application abstracts).



#### References

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- 2. The Alliance Program Book, 2013
- B. NIH databases: RePORTER, QVR, RCDC, PubMed
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#### Acknowledgements

- NCI Office of Cancer Nanotechnology Research (OCNR)
- 2. NCI Office of Science Planning and Assessment (OSPA)
- 3. NIH Office of Portfolio Analysis (OPA)
- 4. Evaluation Set-Aside (ESA) Program funding (2013)

